DEPARTMENT OF THE ARMY
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WRAMC Pamphlet
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Medical Services
HUMAN BIOLOGICAL SPECIMEN BANKING

1. HISTORY.

a. This is a new Walter Reed Army Medical Center pamphlet.

b. The Human Biological Specimen Banking (HBSB) Policy was developed by a subcommittee of the Human Use Committee (HUC), Walter Reed Army Medical Center (WRAMC). The HBSB Subcommittee first convened in November 2001 and met several times to formulate a draft policy that was reviewed, revised, and approved by the subcommittee in September 2002. This policy was reviewed and discussed by the Human Use Committee at the 12 November 2002 meeting and adopted for a period of 6 months. A copy dated 22 November 2002 was subsequently posed in the Department of Clinical Investigation (DCI), WRAMC Web-site. The HUC approved the HBSB policy on 24 June 2003 with minor changes and recommend it to the Command for official policy approval.

c. The HBSB Subcommittee included Chairpersons and Co-chairpersons of the HUC, Chief of the Endocrinology Service (a principal investigator with an approved HBS/tissue bank), Chief of the Nursing Research Service, Chief of the Department of Pathology and Area Laboratories, Chief of the Department of Clinical Investigation, and a non-WRAMC affiliated member of the HUC from the School of Medicine, Uniformed Services University of the Health Sciences.

2. APPLICABILITY.

a. Although this policy is worded as "HBS/tissue," "HBS/tissue specimen," "HBS/tissue bank," or "HBS/tissue sample," guidelines are applicable to all human biological specimens (HBS).

b. The policy applies to all WRAMC investigators who wish to bank HBS/tissue or use the samples from an approved HBS/tissue bank for research purpose.

c. In general, source of HBS/tissue may be obtained for research studies through following two mechanisms:

(1) Acquired from the shelf: existing pathological specimens which were collected prior to there being any interest in using them for research activities and stored exclusively for clinical care purposes.

(2) Prospectively collected from subjects for research purposes, with the HBS/tissue collected either as an excess specimen from a surgical procedure, or obtained according to a research plan.

d. This policy applies to research protocols using the mechanism described above in paragraph 2-c(2). An approved protocol with an informed consent is required for banking such prospectively collected specimens.

e. Research protocols utilizing the mechanism cited in paragraph 2-c (1) will follow the regulations for existing specimens described in the DCI's Standard Operating Procedure (SOP) for review and approval. However, some issues discussed in this policy may also be applicable to research protocols using mechanism cited in paragraph 2-c(1).

3. PURPOSE. To provide regulatory guidance for Walter Reed Army Medical Center (WRAMC) researchers who prospectively collect, store, and distribute human biological specimens (HBS), such as tissue, blood, urine, organs, hair/nails, cells, or fluid for research purposes (note: list is not all inconclusive of human biological specimens).

4. REFERENCES.

a. Army Regulation 40-38, Clinical Investigation Program

b. Genetic Testing Policy, Department of Clinical Investigation, WRAMC

c. Standard Operating Procedure, Department of Clinical Investigation, WRAMC

d. Title 21, Code of Federal Regulations, Part 50, Food and Drug Administration – Protection of Human Subjects

e. Title 21, Code of Federal Regulations, Part 56, Food and Drug Administration – Institutional Review Boards

f. Title 45, Code of Federal Regulations, Part 46, Department of Health and Human Services – Protection of Human Subjects

g. Title 45, Code of Federal Regulations, Parts 160 & 164, The Health Insurance Portability and Accountability Act

5. INSTITUTIONAL REVIEW BOARD (IRB) REVIEW. IRB review and approval of all prospective "HBS/tissue-banking" protocols will proceed as per local, military, and Federal regulations as listed in the DCI Standard Operating Procedure for Clinical Investigation Committee and Human Use Committee. Issues of genetic testing should comply with DCI Genetic Testing Policy.

6. SCOPE.

a. Definitions (Paragraph 7).

b. Type of Banking Protocols (Paragraph 8).

c. Ownership and Control of HBS/tissue (Paragraph 9).

d. Responsibilities of the HBS/tissue Bank PI (Paragraph 10).

e. Identification of HBS/tissue (Paragraph 11).

f. Linkage of Clinical Data with HBS/tissue (Paragraph 12).

g. HBS/tissue Bank Storage and Disposal at WRAMC (Paragraph 13).

h. Maintaining HBS/tissue Bank Inventory List (Paragraph 14).

i. Maintaining HBS/tissue Bank Database for Individual HBS/tissue (Paragraph 15).

j. Type II and Type III HBS/tissue Bank Protocols or "Master" Protocols (Paragraph 16).

k. Type IV protocols or "Sub-protocols" (Paragraph 17).

l. Secondary Use and Consent for Secondary Use by WRAMC and Non-WRAMC (external) Investigators (Paragraph 18).

m. Storage and Inventory by Non-WRAMC Investigators (Paragraph 19).

n. Tertiary Transfer of HBS/tissue by Secondary PIs Outside of WRAMC (Paragraph 20).

o. Cooperative Oncology Group HBS/tissue Banks (Paragraph 21).

p. Access to WRAMC HBS/tissue Stored at Non-WRAMC Sites (Paragraph 22).

q. Necessary Components of Research Protocol and Consent Form (Paragraph 23).

r. Review and Approval Process (Paragraph 24).

7. DEFINITIONS.

a. SPECIMEN: The term "specimen" refers to the entire HBS/tissue from a given individual that is collected and stored in a HBS/tissue Bank.

(1) *Human Biological Specimen*: any material derived from human subjects, such as blood, urine, HBS/tissue, organs, hair/nails, or any other cells or fluid, collected for research purposes or as excess from diagnostic or therapeutic procedures.

(2) *Identified HBS/tissue Specimens*: HBS/tissue specimens held in a HBS/tissue bank that are either directly labeled with personal identifiers, or indirectly linked to them by a code.

(3) *Unidentified HBS/tissue Specimens*: HBS/tissue specimens held in a HBS/tissue bank that has no linkage with identifiers either directly or indirectly coded. Personal identifiers were either not originally collected, were not maintained, or were irrevocably removed. Identity of the source of specimens is forever unknown.

b. SAMPLE: The term "sample" refers to the small amount of HBS/tissue that is removed from the individual specimen, and supplied to the PI for research analysis or testing.

(1) *Anonymous or "Unidentified" Samples*: samples of unidentified HBS/tissue specimens supplied by a HBS/tissue bank.

(2) *Anonymized or "Unlinked" Samples*: HBS/tissue samples obtained from an identified HBS/tissue bank that have been de-identified, or stripped of identifiers per the Health Insurance Portability and Accountability Act (HIPAA) privacy regulation, before issuance to the investigator. No possible linkage to the source of the sample is possible.

(3) *Coded, "Linked", or "Identifiable" Samples*: samples provided by the HBS/tissue bank to the investigator identified by a code only (not an identifier per HIPAA), that can potentially be linked to the source of the sample.

(4) *Identified Samples*: HBS/tissue samples from identified specimens supplied by the HBS/tissue bank with a personal identifier, such as name, social security number, patient identification are not allowed.

c. INVESTIGATORS.

(1) *Principal Investigator* (PI): The principal investigator has overall primary responsibility to ensure that the research study is conducted in a manner that is in accordance with the federal, army, and local guidelines and regulations that govern research at WRAMC. Staff assigned to or employed by WRAMC, that have professional privileges at WRAMC and who are performing research within the scope of their professional privileges, and have completed the required WRAMC Research Course, may be the PI of a banking protocol. See DCI template (Human.doc) for a list of PI responsibilities.

(2) *Collaborator or External Investigator*: A non-WRAMC affiliated investigator can only be a collaborator of a WRAMC investigator and not a principal investigator.

d. USE OF THE SPECIMENS AND SAMPLES

(1) *General Use*: HBS/tissue specimen saved for future research, the objectives of which are as yet undetermined at the time of HBS/tissue collection.

(2) *Specific Use*: HBS/tissue specimen collected and/or saved for research described specifically in the objective of the protocol and in the consent form.

(3) *Primary Use*: Sample used by Principal Investigator (PI) of the protocol under which the HBS/tissue was originally approved to be banked.

(4) *Secondary Use*: Sample use of banked HBS/tissue by an investigator other than the primary investigator, with the knowledge/consent of primary investigator.

(5) *Tertiary Use*: Use of sample from banked HBS/tissue by an investigator other than the primary investigator, requiring off-site transfer of sample by an investigator other than the primary investigator.

e. HBS/TISSUE BANK

(1) *HBS/tissue Bank*: HBS/tissue storage repository or facility at WRAMC or at a WRAMC-recognized off-site location that operates in accordance with WRAMC regulations. It contains human biological specimens collected under WRAMC-approved research protocols.

(2) *WRAMC-Sponsored HBS/tissue Bank*: a HBS/tissue bank established at WRAMC, by a WRAMC PI, whose protocol for HBS/tissue collection and storage has been approved by DCI and the HUC.

(3) *WRAMC-Recognized HBS/tissue Bank*:

(a) A HBS/tissue bank located at a non-WRAMC facility that has an established HBS/tissue banking policy, which has been reviewed and found acceptable by the WRAMC HUC with safeguards meeting the requirements for a WRAMC-sponsored HBS/tissue bank. Examples of WRAMC-Recognized HBS/tissue Bank would be Oncology Group HBS/tissue Banks, such as CALGB. Bank sites that are not acceptable include non-academic, for-profit institutions such as pharmaceutical companies or commercial HBS/tissue banks. WRAMC-recognition does not indicate assurance that safeguards are in place, only that standard of operation documents have been reviewed and deemed acceptable.

(b) A Memorandum Of Understanding (MOU) may be required to be established between the institutions sponsoring such HBS/tissue banks and WRAMC. The institutions may include federal facilities (i.e., USUHS, WRAIR, NIH, NNMC, VA, etc) and other non-federal sites.

Note: Such MOUs are especially important when substantial numbers of samples (e.g., >10) are to be contributed from WRAMC. Exceptions to the MOU process may include the Oncology Group HBS/tissue banks (See Paragraph 21). More details regarding this appear in Paragraphs 19, 20, and 22.

8. TYPE OF HBS/TISSUE BANK PROTOCOLS. There are 4 potential types of protocols involving human biological specimen banking (hereafter described as "HBS/tissue banking").

a. Type I: Type I protocols obtain HBS/tissue specimens for purposes of a given research study. The specimens are stored until analysis/publication/end of protocol occurs, and the unused specimens are then destroyed. If the specimens have IRB approval to be sent to a non-WRAMC facility for analysis, the excess specimens (if any) must be destroyed appropriately or returned to WRAMC for disposal. Type I specimens are not considered to be "banked", and the remainder of this policy does not apply to them.

b. Type II: Type II protocols have well-defined research objectives and collect human biological specimens for the purposes of the given research study followed by saving or "banking" the specimens for future/potential research either related or unrelated to the objectives or disease studied.

c. Type III: Type III protocols obtain specimens with or without clinical information (one-time or ongoing) and store or "bank" the specimens for potential future studies whose objectives are to be determined at a later point in time. These types of "HBS/tissue banking" protocols may be referred to as "master HBS/tissue banking" protocols. These protocols may involve general or specific types of HBS/tissue (i.e., breast HBS/tissue only vs. several other HBS/tissues collected). In some instances, a protocol is submitted including a collection of HBS/tissue specimens not for the given research protocol but purely to bank them for future research use. This type of protocol may be considered as a Type III protocol of HBS/tissue banking.

d. Type IV: Type IV protocols are sub-studies of a Type II or III protocol. Type IV protocols are hypothesis driven studies using HBS/tissue under Type II or III HBS/tissue banking protocol. HBS/tissue used under Type IV protocols may not be "banked" secondarily. The objective of using the HBS/tissue in this type of protocol is similar to the Type I protocols.

9. OWNERSHIP AND CONTROL OF HBS/TISSUE.

a. At WRAMC, investigators and staff are not "owners" of the HBS/tissue. As a federal facility, WRAMC is responsible for controlling the disposition of HBS/tissue collected for clinical or research purposes, and making decisions about use or non-use. The PI is the steward of the HBS/tissue.

b. WRAMC is authorized to "dispose" of all excess HBS/tissue not needed for clinical reasons (per SF 522, Request for Administration of Anesthesia and for Performance of Operations and Other Procedures). Thus, WRAMC controls excess human HBS/tissue obtained for clinical reasons, and is authorized to dispose of it in an established manner.

c. In a research context, the subject and investigator both have control of HBS/tissue based on the agreement reached during the informed consent process, and documented in the consent form.

d. All protocols that employ HBS/tissue banking of biological specimens obtained from patients or subjects at WRAMC (i.e., Types II-IV) must have a WRAMC staff member as a PI on the master banking protocol, and all research studies generated must be approved by the WRAMC HUC/IRB.

e. HBS/tissue will not be supplied to a non-WRAMC institution for banking purposes, unless:

(1) An approved WRAMC protocol exists with a clear plan specifying collection process, along with a consent form indicating the use and safeguard of the specimens, AND

(2) The HBS/tissue bank is a WRAMC-recognized-HBS/tissue-bank.

f. No HBS/tissue will be transferred for a secondary or tertiary use unless it is approved by the HUC. Especially, if secondary or tertiary use is for a non-WRAMC investigator, no HBS/tissue may be released unless it is under the provisions of an MOU with the other institution ensuring appropriate use and confidentiality protection of the samples. The other institution's IRB must approve the use of such samples.

g. If HBS/tissue is sent to a non-WRAMC institution for testing or use as defined in a protocol, once the specific analyses are performed, the remainder of the specimens must be destroyed or returned to the WRAMC for disposal (destruction or re-storage).

10. RESPONSIBILITIES OF THE HBS/TISSUE BANK PI. In addition to the responsibilities of PIs under the present regulations (45 CFR 46, 21 CFR 50, 56, AR 40-38, and local WRAMC Policy), the PI will:

a. Serve as the steward of the approved HBS/tissue bank and be responsible to answer CIC/HUC or other regulatory offices questions at any time.

b. Be available for appointment as a HBS/tissue-banking consultant at the HUC/CIC meeting for reviewing other HBS/tissue banking protocols.

c. Ensure that the HBS/tissue bank follows standard procedure for HBS/tissue storage, processing, and disposal (see Paragraph 13).

d. Maintain a HBS/tissue Bank Inventory List (see Paragraph 14).

e. Maintain a HBS/tissue bank database to:

(1) Ensure subjects' options as outlined in the consent form are followed;

(2) Track entries, removal, availability, and distribution of the specimens;

(3) Report all changes to DCI and to subjects as appropriate (see Paragraph 15).

f. Not release HBS/tissue to any WRAMC or non-WRAMC investigator without a WRAMC approved protocol (and MOU, if required).

g. PIs with General Use HBS/tissue banks should facilitate the use and access of the HBS/tissue by WRAMC investigators over the needs of outside investigators. They do not have the right of refusal to WRAMC investigators with a DCI approved protocol (i.e., Type IV protocol), if the HBS/tissue exists. However, they do have the right to assess the potential impact of a given protocol on the bank. Therefore, PIs of master HBS/tissue bank protocols will be required to issue impact statements for Type IV applications.

h. PIs with Specific Use HBS/tissue banks (i.e., breast, prostate, thyroid) should facilitate the use of HBS/tissue by other investigators provided that new use is approved by HUC and use is not detrimental to the HBS/tissue bank.

i. Departing PIs on HBS/tissue banking protocols will:

(1) Officially transfer the protocol to a new PI, or

(2) Close the protocol and transfer the existing banked HBS/tissue and all relevant documents to an existing WRAMC General Use HBS/tissue bank, or

(3) After review by DCI and HUC, properly destroy the HBS/tissue before leaving WRAMC.

11. IDENTIFICATION OF HBS/TISSUE.

a. At Bank: HBS/tissue specimens within the bank may be unidentified or identified. All identifiable specimens within the banks should be stored with a unique code number, which may be linked to personal information. The code must not be part of any of the 18 HIPAA identifiers (e.g. Social Security Number, initials, zip code, etc). The master list which links the code numbers must be kept in a secured place, (such as password-protected or locked file), and be controlled by the PI or a single authorized designee. Anonymized and unlinked samples are samples where all identification is stripped off and cannot be linked to any personal information.

b. When Released for Research Use: There are two possible ways that identified bank HBS/tissue samples may be released for Primary or Secondary Use:

(1) Anonymized and Unlinked samples.

(2) Coded and Linked samples.

c. Identified samples with directly identifiable personal information are not permitted for distribution.

12. LINKAGE OF CLINICAL DATA WITH BANKED HBS/TISSUE.

a. Banked HBS/tissue may be linked with clinical information after IRB approval. Clinical data may be either obtained once prospectively or over time for ongoing collection of specimens depending on what method was approved by IRB.

b. Only coded or de-identified clinical information and HBS/tissue may be issued to secondary use investigators.

13. HBS/TISSUE BANK STORAGE AND DISPOSAL AT WRAMC.

a. Individual WRAMC HBS/tissue bank PIs are responsible for following the standard operating procedures at WRAMC for processing and storing the HBS/tissue. PIs are required to follow Paragraph

11 of this policy for protecting the confidentiality of HBS/tissue.

b. Specimen storage may be up to 20 years period provided there is an endowment or other system in place to preserve and protect the HBS/tissue for the specified duration. However, the protocol is subject to the continuing review and approval at least once annually by the HUC. A longer storage time may be approved by the HUC.

c. If research subjects decide that they no longer wish to bank their HBS/tissue, it must be disposed in an appropriate manner by the PI, i.e., following the standard operating procedures (SOP) used at WRAMC. All disposal of HBS/tissue must be reported to DCI, documented in the HBS/tissue database, and reported to the subject(s) who requested to have their specimen removed.

14. MAINTAINING A HBS/TISSUE BANK INVENTORY LIST.

a. WRAMC HBS/tissue bank PIs are required to create and maintain an inventory for documentation with DCI that summarizes information about the master banking protocol and any subsequently approved "sub-protocols". This inventory list should be simple and should not contain individual tracking records for samples. Tracking of samples should be done in a separate database (See Paragraph 15).

b. The PIs should report any banking changes to DCI as they occur and provide DCI a copy of the inventory list at the time of Annual Progress Report.

c. The inventory list should include the following components, as appropriate:

(1) Inventory code.

(2) DCI Protocol Work Unit Number (banking protocol).

(3) DCI Protocol Type (Type II or Type III for banking protocol, Type IV for subprotocol)

(4) PI – name, rank and department/service.

(5) Date of the HUC approval for the banking protocol.

(6) An informed consent was required (yes/no).

(7) Date of most current consent form approved.

(8) Sample size approved.

(9) Site of Storage (e.g. WRAMC, USUHS, NCI, etc.).

(10) Study site.

(11) Specify the coding system of HBS/tissue specimens at bank. (Note that all specimens should be "coded" for all banks and could be "anonymized" for subsequent use.)

(12) Type and number of HBS/tissue collected (e.g.: "Thyroid"; 2 samples—1.6 and 2.7 grams or "serum"; 5 samples—0.5 cc each).

(13) Authorizations approved by the HUC:

(a) Genetic testing (yes/no).

(b) General use or Specific use.

(c) List of the research scope – types of diseases or conditions authorized for future studies.

(d) Tertiary use authorized (yes/no).

(e) WRAMC use only or extramural use permitted.

(14) For each subsequent sub-study (i.e., Type IV protocol) for which use of this HBS/tissue is authorized, extend the inventory list to include information similar to above items as cited in paragraphs 14-c(1) – 14-c(13).

(15) Other: Note the information of PI change or other changes.

d. At a minimum the inventory list needs to be updated at the time of HBS/tissue use, at the time of HBS/tissue destruction, at the time of approval of Type IV protocols for which the HBS/tissue will be used (by time of issuance of memorandum approving the protocol), and at the time of the Annual Progress Report.

15. MAINTAINING A HBS/TISSUE BANK DATABASE FOR INDIVIDUAL HSB/TISSUE.

a. The above inventory summary for documentation for DCI is not inclusive of all required data to be kept in a HBS/tissue bank database by the PI.

b. PIs with WRAMC approved HBS/tissue bank are responsible for creating and maintaining an independent database to track individual HBS/tissue specimens entered in the databank. This database may be reviewed at any time by the HUC/IRB or DCI.

c. The database for each HBS/tissue should include the following fields, as appropriate:

(1) Inventory code - same for all records in the bank.

(2) PI identification (i.e., name, rank and department/service) – same for all records, except when there is a PI change.

(3) HBS/tissue identifier code.

(4) Date of informed consent signed by the subjects.

(5) Date of the HBS/tissue collected.

(6) HBS/tissue type and number presently existing in the bank, (e.g., "Thyroid"; 2 samples—1.6 and 2.7 grams).

(7) Authorizations by subjects according to the consent form:

(a) Genetic testing (yes/no).

(b) General use or Specific use.

(c) List of the research scope - types of diseases or conditions authorized for the future studies.

(d) Secondary use authorized (yes/no).

(e) Tertiary use authorized (yes/no).

(f) WRAMC use only, or non-WRAMC use permitted.

(8) Withdrawal requested by the subjects (yes/no), date requested, date of HBS/tissue withdrawal, date reported to the subjects confirming such withdrawal and destruction.

(9) For each Type IV protocol, authorized use of the HBS/tissue, including DCI work unit number, date of HBS/tissue removal, amount removed, to whom it was given (name, rank, institution site), how it was given (coded or de-identified), type of the disease application, genetic testing (yes/no), and date of destruction or return of excess samples.

(10) If approved by the HUC for the use of clinical data, the PI may include additional fields for clinical data or create a separate database for clinical data with only a code number that links to the HBS/tissue bank database.

16. TYPE II AND TYPE III HBS/TISSUE BANKING PROTOCOLS OR "MASTER" PROTOCOLS.

a. Type II and Type III protocols are defined in Paragraphs 8-b. and 8-c.

b. Type II and Type III protocols are prospective HBS/tissue banking protocols. Whether with or without clinical data, these protocols must be reviewed by the HUC/IRB, there must be informed consent, and the consent process must include as much detail as possible regarding the potential future use of the HBS/tissue specimens:

(1) Scope of the General Use and/or Specific Use,

(2) Primary Use by the HBS/tissue bank PI,

(3) Secondary Use by other investigators if any,

(4) Whether HBS/tissue will be sent out to other institutions for storage, for collaboration, etc.,

(5) Whether any genetic testing will be conducted, and

(6) Whether or not subjects will agree to be contacted for subsequent consent to additional studies (see also Paragraph 23).

c. Any protocols involving potential genetic testing must follow the DCI guidelines for protocols involving genetic testing.

d. To maintain subject confidentiality, it is necessary to provide subjects information about possible future uses of their HBS/tissue at the time of original consent. The subject should be able to specify their views on whether the HBS/tissue can be used exclusively for the protocol in question, for other studies dealing with diseases affecting the organ from which the HBS/tissue came from, or for studies dealing with broad diseases affecting other organ systems or humanity as a whole. It is not recommended to have a clause indicating that patients will be re-consented for future studies, because this may involve re-linking of the subject's personal information with the HBS/tissue. It is also logistically impossible to achieve.

e. Provide check-off options at the end of the consent form to allow subjects to define restrictions to future use regarding the issues of specific disease only, any other disease, only the PI, other secondary investigators; genetic testing or not.

17. TYPE IV PROTOCOLS OR "SUB-PROTOCOLS".

a. WRAMC HBS/tissue bank investigators will need to submit a new protocol (i.e., Type IV protocol) for each "experiment" using banked HBS/tissue not described in the original "banking" protocol.

b. All Type IV protocols are sub-studies of a "master" HBS/tissue bank protocol. These Type IV "sub-protocols" must be approved by the HUC and/or CIC.

c. Type IV protocols should include specific research objectives. The protocol application should be specific as to number of specimens needed, clinical features, clinical data needed, and the time frame of the HBS/tissue collected for the use in this study.

d. Type IV protocols may not bank the excess HBS/tissue secondarily. All excess HBS/tissue must be returned to the original source or be destroyed per WRAMC SOP.

e. If the HBS/tissue samples are sent to a non-WRAMC institution for testing or use as approved in the protocol, specify where, to whom and how the HBS/tissue will be sent. Once the specific analyses are performed, the remainder of the specimens must be destroyed or returned to the WRAMC for disposal (destruction or re-stored).

f. Subject consent will not be required for each use in an experiment, unless the original consent agreement indicates that re-consent is required.

g. Type IV protocols with de-identified specimens to investigators (secondary PI) not involved in the banking process may be determined by the DCI for exemption from the IRB review.

18. SECONDARY USE AND CONSENT FOR SECONDARY USE BY WRAMC AND NON-WRAMC (EXTRAMURAL) INVESTIGATORS.

a. No HBS/tissue may be transferred for a secondary use without the approval of the HUC. Especially, if secondary use is for a non-WRAMC investigator, no HBS/tissue may be released unless it is under the provisions of an MOU with the other institution ensuring appropriate use and confidentiality protection of the samples, and that investigator's IRB has approved the use of such samples.

b. Secondary use PIs wishing to access the HBS/tissue will need to approach the master bank PI directly, and include him/her as an associate PI, if appropriate.

c. An impact statement is required from the investigator who operates the HBS/tissue bank for all secondary use protocols.

d. Subject consent will not be required for each use in an experiment, unless the original consent agreement indicated that re-consent is required.

e. Secondary use protocols can only use the banked HBS/tissue that is in accordance with the original wishes of the subject, as outlined in the consent form.

f. Secondary use protocols need to be prepared according to Type IV protocols guidelines.

g. Non-WRAMC (extramural) investigators who wish to use WRAMC banked HBS/tissue will be "collaborators" to a WRAMC HBS/tissue bank PI, and will receive only de-identified HBS/tissue.

Note: Whenever possible, analysis of data developed from the HBS/tissue and associations with clinical data will be done by the WRAMC investigator (i.e., minimal raw clinical data will be given to outside investigators).

h. The smallest necessary portion possible of an individual subject's HBS/tissue should be released (i.e., unstained slides, etc) for any secondary use.

19. STORAGE AND INVENTORY BY NON-WRAMC INVESTIGATORS.

a. For storing HBS/tissue by non-WRAMC investigators, a WRAMC protocol and a MOU are required to be established between the institution sponsoring the HBS/tissue bank and WRAMC (see Paragraph 22-e). Such MOUs must include the provisions regarding final disposition of HBS/tissue when the studies are completed and no longer necessary. Documentation of destruction of samples must be made available to WRAMC DCI via official letter from the institution or samples must be returned to the Research Operation Service of the Department of Clinical Investigation, WRAMC for disposal. As appropriate, Path slides or blocks should be returned to DPALS Anatomic Pathology Service. Distribution to third parties is not allowed.

b. Storage and inventory must be described in detail in the protocol.

c. Storage may not exceed 5 years, unless an addendum to the protocol by the WRAMC PI is submitted and approved.

20. TERTIARY TRANSFER OF HBS/TISSUE BY SECONDARY PIs OUTSIDE OF WRAMC.

a. Generally, secondary investigators (either WRAMC-based or not) may not make transfers of HBS/tissues to other investigators. Excess HBS/tissue must either be returned to WRAMC, or destroyed. This must be specified in the protocol.

b. Exceptions to the above policy are dealt with in 20-c. below, and in Paragraph 22. These allow for MOUs establishing HBS/tissue banks at other academic institutions with WRAMC HBS/tissue, and for dealing with the cooperative oncology group HBS/tissue banks.

c. MOUs may be developed between the command and other institutions to establish HBS/tissue banks containing WRAMC HBS/tissue at the other institutions. Such protocols are still subject to IRB approval, and WRAMC investigators should have preferential access to the HBS/tissue. Generally, these MOU-established banks should meet the requirements of the HBS/tissue bank policy at WRAMC.

21. COOPERATIVE ONCOLOGY GROUP HBS/TISSUE BANKS

a. Generally, HBS/tissue from WRAMC subjects may be permanently deposited in Cooperative Oncology Group HBS/tissue banks (such as GOG, SWOG, POG, and CALGB) provided it is a WRAMC-recognized HBS/tissue bank, subject to the requirements of the protocol and COG HBS/tissue banking policy, which may include tertiary transfer of HBS/tissue. The original protocol for collection of such HBS/tissue must have a WRAMC PI, and WRAMC IRB approval; however, subsequent HBS/tissue dispersal will be at the discretion of the COG, and not subject to further WRAMC IRB review, unless the PI is a WRAMC PI, or the IRB makes an exception to this policy, and places specific requirements on the COG.

b. A copy of the COG HBS/tissue banking policy must be submitted to the WRAMC IRB at the time of initial review, so that the IRB may make an informed decision about 20.a. above.

22. ACCESS TO "WRAMC" HBS/TISSUE STORED AT NON-WRAMC SITES BY MOU.

a. In the event the WRAMC IRB approves a HBS/tissue banking protocol, which is established by MOU at a non-WRAMC site, WRAMC PIs should have preferential access to the WRAMC HBS/tissue stored there.

b. The MOU should establish how this preferential access will be implemented.

c. The MOU should also be reviewed and approved by the IRB, prior to the approval by the Commander.

d. The MOU should specify in detail how the HBS/tissue will be stored, where it will be stored, for how long, and the actual physical precautions taken to secure and store/preserve the HBS/tissue. (Long periods of storage must have detailed plans in place for the accomplishment—if the plan is to store HBS/tissue for 50 years, there must be an institutional commitment and physical plant commensurate to such a program, and a detailed plan).

e. The MOU must describe the plan for distributing banked HBS/tissue to secondary investigators, and must have safeguards similar to those required for a WRAMC-sponsored HBS/tissue bank.

f. Provision must be made in the MOU for providing to the WRAMC IRB and DCI regular information regarding the amount, identity, and release of WRAMC HBS/tissue in a format similar to that of the WRAMC HBS/tissue Inventory, (see Paragraph 14-a. thru 14-d.), so that we may account for HBS/tissue disposition, and allow potential WRAMC investigators to know of the types and amount of HBS/tissue available to them for research.

23. NECESSARY COMPONENTS OF PROTOCOL AND CONSENT FORM.

a. The consent form should follow the guidelines in this policy and other existing WRAMC and Dept of Army Guidelines, including DCI Genetic Testing Policy, if applicable.

b. The protocol should detail the following:

(1) What HBS/tissue form will be stored (HBS/tissue; fixed HBS/tissue; cDNA; DNA; proteins, etc).

(2) Site of storage.

(3) How HBS/tissue will be stored (security; physical conditions; compliance with OSHA regulations).

(4) Who will have access to HBS/tissue, to clinical information, to linkages.

(5) How confidentiality will be protected—clinical and identifier information flow, what type of identifiers/codes, de-identification.

(6) How the HBS/tissue will be used (as specific as possible).

(7) Whether there will be genetic studies.

(8) Whether there will be any commercial interest such as, developing cell lines, etc.

(9) Will there be secondary or tertiary use.

(10) Length of time of storage.

(11) Whether or not subject will be contacted and consented for future uses.

(12) Conditions under which HBS/tissue will be destroyed and how.

(13) How subjects may withdraw from bank (HBS/tissue, links, codes, and clinical information all destroyed; or clinical information, codes, and links destroyed, leaving completely unidentified HBS/tissue).

c. In the consent form, the details given in Paragraph 23-b. should be disclosed, and consideration given to giving the subject the option of determining "HBS/tissue use" at the time of original consent. This would be done in a series of YES/NO questions, which could include decisions regarding genetic testing, general use. These questions are best limited, as multiple options make future handling more difficult—especially with regard to confidentiality.

d. In Type II studies, where HBS/tissue banking may be an optional part of the protocol for the subject, the subject must be able to indicate YES/NO whether he/she wishes HBS/tissue to be banked.

e. Explanations of restrictions (if any) on guarantees of confidentiality. For example, confidentiality could be lost if subject is also guaranteed to receive information about the results of studies involving their sample/clinical data.

24. REVIEW AND APPROVAL PROCESS.

a. All HBS/tissue banking proposals (i.e., Type II, III, and IV protocols) are subject to IRB/HUC review.

b. Type II and III HBS/tissue Bank Protocols must be reviewed by the full IRB and not by "expedited" review.

c. At HUC and CIC meetings at which "HBS/tissue banking" protocols are discussed (i.e., Type II, III, or IV studies), a "HBS/tissue-banking" consultant (similar to an oncology consultant) will be present to provide expert advice. The consultant would be one of the PIs with either an active HBS/tissue banking protocol, or a PI with considerable previous experience with HBS/tissue banking protocols.

d. The PI or Associate PI of a Type II or III protocol may submit sub-studies using the HBS/tissue banked under the "master" protocol. These sub-studies may be reviewed by expedited process, but are not "exempt".

e. For the purpose of HUC/IRB oversight of such HBS/tissue banking protocol, the length of HBS/tissue protocol will be initially approved with a continuing review for 5 years as all other WRAMC protocols. However, the protocol may be extended for additional 5 years by an addendum, or a new protocol may be submitted if deemed necessary by the HUC/IRB.

25. EFFECTIVE DATE AND IMPLEMENTATION. This policy is effective immediately. The Chief, Department of Clinical Investigation shall issue implementing guidance.

The proponent agency of this publication is the Office of the Chief, Department of Clinical Investigation, Walter Reed Army Medical Center. Users are invited to send suggestions and comments on DA Form 2028 (Recommended Changes to Publications) to Commander, Walter Reed Army Medical Center, ATTN: MCHL-CL, 6900 Georgia Avenue, NW, Washington, DC 20307-5001.

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